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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,416	05/19/2005	Jaume Pinol Ribas	Q-87778	7473

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EXAMINER
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,416	RIBAS ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-29* is/are pending in the application.

4a) Of the above claim(s) *18 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.Applicants' submission filed on 1/27/2009 has been entered. Claims 13 and 24 have been amended.

2. Claims 13-29 are pending. Claims 13-17 and 19 are under consideration. Claims 18and 20-29 are withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

3. Applicants' arguments in regard to election of 11/01/2007 are acknowledged.

Applicants argue:

- *Reimer et al.* clearly do not disclose a mutant strain whhich comprises a mutation in at least one region of an *apxIA and apxIIA* gene, much less within a transmembrane domain of such, as is the special technical feature linking the claims of Groups I-IV. As discussed previously, Reimer *et al.* disclose a *wild-type* strain (J45) which synthesizes and secretes exotoxins ApxI and ApxII, a mutant with the C, B, A, and D genes *(apxICABD* operon) of ApxI *completely deleted* (mIT4-H), a mutant in which the *deleted apxICABD operon is restored* (MIT4-H/pJFFS00), and a mutant in which the *B and D genes (apxIBD operon) for ApxI are restored.* None of the aforementioned strains is immunogenic and non-haemolytic (avirulent), as claimed, because strains J45 and miT4-H/pjFFS00 have the whole genetic information and are *virulent* strains, strain mIT4-H is a *non-immunogenic* and avirulent chemical mutant, and strain mIT4-H/pJFFS01 has genetic modifications and is *non-immunogenic* and virulent. Thus, as would be appreciated by those of skill in the art, the special technical feature linking

> Groups I-IV, namely the presence of at least one mutation in a transmembrane domain-encoding segment of the *apxIA* gene, and optionally at least one mutation in a transmembrane domain-encoding segment of the *apxIIA* gene, is not disclosed, nor even remotely contemplated by Reimer *et al.* For this reason alone, Restriction is improper.

This is not found persuasive. Reimer et al teaches also teach mutations in the apxIA and apxIIA and the apxI CABD operon and non-haemolytic strains (see abstract and page 198). Additionally each group of I-IV as mentioned in the restriction mailed 10/02/2007 has a special technical feature that is not required for the other groups.

The special technical feature of group I is a strain of *Actinobacillus pleoropneumoniae* APP.

The special technical feature of group II is a strain of *Actinobacillus pleoropneumoniae* CECT 5985.

The special technical feature of group III is a strain of *Actinobacillus pleoropneumoniae* CECT 5994.

The special technical feature of group IV is a method of obtaining an organism.

The requirement is still deemed proper and is therefore made FINAL.

Rejections Maintained

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent
>
> in the United States.

5. Rejection of claims 13-17 under 35 U.S.C. 102 (b) made in paragraph 12 of the office action mailed 2/13/2008 is maintained.

The rejection was as stated below:

Claims 13-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by MacInnes et al. US 6,019,984

Claims are drawn to an immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strain comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene.

MacInnes et al. teach immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strains comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene (see abstract and claims and columns 1-4). MacInnes et al. teach deletion mutations, apxIA and apxIIA (see claims 6-12 and column columns 3 and 4 and figures). As to product of claim 19 and product of MacInnes et al. they are indistinguishable (see columns 13-14). MacInnes et al. teach do not explicitly teach nucleotides 886 to 945 of apxIA gene, however, such limitation would inherent in the full sequence of apxIA taught by MacInnes et al. The prior art anticipates the claimed invention.

Applicants' arguments filed 6/12/2008 have been fully considered but they are not persuasive.

The applicants argue:

- The Examiner appears to believe that MacInnes *et al.* disclose immunogenic, non-hemolytic *Actinobacillus pleuropneumoniae* strains comprising a mutation in at least one region of the *apxIA* gene and optionally a mutation in at least one region of the *apxIIA* gene, citing the Abstract, claims, and columns 1-4 in support of such a contention. MacInnes *et al.* is also alleged to disclose deletion mutations of *apxIA, and apxIIA,* citing Claims 6-12, columns 3 and 4, and the figures of MacInnes *et al.* However, neither the portions of MacInnes *et al.* cited in the rejection, nor any other portion of MacInnes *et al.* for that matter, discloses an *Actinobacillus pleuropneumoniae* strain comprising a mutation in a

transmembrane domain-encoding segment
of the *apxIA* gene, and optionally a mutation in a transmembrane domain-encoding segment of the *apxIIA* gene, either explicitly, or inherently, much less that the transmembrane domain- encoding segment of *apxIA and apxIIA* corresponds either to nucleotides 886 to 945, to nucleotides 697 to 759, or to nucleotides 1105 to 1215, as currently claimed. The Abstract, claims, and columns 1-4, which are alleged to disclose as such, merely discuss different RTX toxins, which include ApxI, ApxII and ApxIII, and contemplate the modification *of Actinobacillus pleuropneumoniae* strains to produce RTX toxins which are "substantially cell-associated." Although strains are contemplated in which ApxI and ApxII are substantially cell-associated, such strains are not expressly described by MacInnes *et al.*

MacInnes teach transposon mutants of different strains and APX toxins from 12 different serotypes of *Actinobacillus pleoropneumoniae* strains (see figures 3, 16, 17, 18 and 19). MacInnes also teach that outer membrane proteins of *Actinobacillus pleoropneumoniae* can be altered by changing the growth conditions (see column 22).

As to amended claim 13 optionally a mutation in a transmembrane domain-encoding segment of the *apxIIA* gene. The claim language using the term optionally does not require a mutation in transmembrane domain-encoding segment of the *apxIIA* gene.

6. Rejection of claims 13, 14, 15, 17 and 19 under 35 U.S.C. 102 (b) made in paragraph 13 of the office action mailed 2/13/2008 is maintained.

The rejection was as stated below:

Claims 13, 14, 15, 17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Prideaux et al. US 6, 0472,183 B2.

Claims are drawn to an immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strain comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene.

Prideaux et al. teach immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strains comprising a mutation in a least in one region of the

apxIA gene and optionally a mutation in a least in one region of the apxIIA gene (see abstract and claims and columns 1-2). Prideaux et al. teach deletion mutations, apxIA and apxIIA (see claims 1-4 and column columns 3 and 4). As to product of claim 19 and product of Prideaux et al. they are indistinguishable (see columns 8, 20 and examples 5-6). The prior art anticipates the claimed invention.

Applicants' arguments filed 6/12/2008 have been fully considered but they are not persuasive.

The applicants argue:

- Although the Examiner maintains the rejection, asserting that Prideaux *et al.* disclose immunogenic, non-hemolytic *Actinobacillus pleuropneumoniae* strains comprising a mutation in at least one region of the *apxIA* gene and optionally a mutation in at least one region of the *apxIIA* gene, citing the Abstract, claims, and columns 1-2, and that Prideaux *et al.* disclose deletion mutations of ApxIA and ApxIIA, citing Claims 1-4 and columns 3 and 4, the Examiner is respectfully requested to note that the claims as examined recited that the mutation occurs within a transmembrane domain of ApxIA, and optionally ApxIIA. Pursuant to M.P.E.P. § 2143.03, "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art." Neither in the portions of Prideaux *et al.* relied upon to support the rejection, namely the Abstract, Claims 1-4, columns 1-4, or in any other portion of Prideaux *et al.* for that matter, is the claimed strain containing a mutation in a transmembrane domain disclosed, expressly or inherently.

Prideaux et al. teach mutated A gene of apxI (see example 4 , column 14) wherein apxI A gene and a Kanamycin resistance gene linked to T5 promoter was resulted in transformants which were Kanamycin resistant and produced white colonies.

As to amended claim 13 optionally a mutation in a transmembrane domain-encoding segment of the *apxIIA* gene. The claim language using the term optionally does not require a mutation in transmembrane domain-encoding segment of the *apxIIA* gene.

New Rejections

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 13-17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claim 13 recites, wherein the transmembrane domain-encoding segment in each *apxIA* gene and *apxIIA* gene corresponds either to **nucleotides 886 to 945**, to **nucleotides 697 to 759**, or to **nucleotides 1105 to 1215** . This is indefinite; applicant should have recited sequence id number representing these specific nucleotides.

The term "optionally" in claim 13 is a relative term which renders the claim indefinite. The term "optionally" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S. Shahnan-Shah whose telephone number is

(571)-272-0863. The examiner can normally be reached on Mon, Wed 12:30-6:30 pm, Thur12:30-4:30pm pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on (571)-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Khatol S Shahnan-Shah/
Examiner, Art Unit 1645
April 11, 2009

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645